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Laboratory of Personality and Cognition

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The fundamental scientific paradigm guiding research in the Laboratory of Personality and Cognition (LPC) is the analysis of individual differences. Few phenomena are more basic than the fact that human beings differ—in health, in rates of aging, in cognitive ability, in personality, in happiness, and in life satisfaction.

The Laboratory of Personality and Cognition (1) conducts basic and clinical research on individual differences in cognitive and personality processes and traits; (2) investigates the influence of age on these variables and their reciprocal influence on health, well-being and adaptation; and (3) employs longitudinal, experimental, and epidemiological methods in the analysis of psychological and psychosocial issues of aging, including health and illness, predictors of intellectual competence and decline, models of adult personality, and correlates of disease risk factors.

The Personality, Stress, & Coping Section conducts basic and applied research on personality as it relates to aging individuals including studies of stress and coping, mental and physical health risks and outcomes, adaptation and well-being. Basic research has centered on a taxonomic model of personality traits and its assessment.

The Cognition Section conducts studies that attempt to distinguish pathological from healthy, age-related cognitive changes in a broad range of cognitive tasks including short-term and long-term memory, visuo-spatial rotation, attention and decision tasks. In addition, structural and functional brain changes are examined using MRI and PET. Studies are performed on regional structural brain changes, especially the hippocampus, and their relationship to cognitive performance and dementia. Regional differences in cerebral blood flow derived from PET studies at rest and during cognitive challenge are related to aging and patterns of cognitive change.

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Recent Publications:

Costa PT, Jr, et al. *Recognition and initial assessment of Alzheimer's disease and related disorders: Clinical Practice Guidelines, No. 19.* 1996; AHCPR Pub. No. 96-0702.

Costa PT Jr, et al. *Eur J Pers* 1998 ;12: 117-134.

Costa PT Jr, et al. In *Advanced Personality.* Barone, DF, ed. Plenum Press: New York, 1998; 103-118.

Biography: Dr. Costa received his undergraduate degree in Psychology from Clark University and his doctorate in Human Development from the University of Chicago. After academic positions at Harvard and the University of Massachusetts at Boston, he joined NIA to inaugurate a Stress and Coping Section. Since 1985 he has been Chief of the Laboratory of Personality and Cognition. His research interests include adult development, personality assessment, and Alzheimer's disease.

The Laboratory of Personality and Cognition addresses the psychology of aging through research on individual differences and intraindividual changes in cognitive abilities and personality dispositions. Its two Sections share use of the BLSA population, a focus on psychometrics and construct validation, and an emphasis on longitudinal research. Some research involves data from both Sections—for example, studies relating Openness to Experience to cognitive abilities, and explorations of brain activation patterns associated with personality factors. Both Sections share a developing interest in the molecular genetic basis of psychological characteristics, and both are concerned with applications of findings for health promotion and disease prevention.

Basic Research in Personality - The Five-Factor Model: Although many theoretical perspectives (including psychoanalytic, behavioral, and humanistic) have been taken on personality, most empirical research is based on trait models that address individual differences in characteristics of the person. A major obstacle to progress in personality psychology for many decades was the inability of psychologists to agree on a taxonomy of traits that would offer a comprehensive yet manageable set of trait constructs. Since 1983, this Laboratory has contributed to a worldwide consensus that the Five-Factor Model provides such taxonomy. The broad factors of Neuroticism, Extraversion, Openness to Experience, Agreeableness, and Conscientiousness appear to encompass most specific traits, and offer a framework for systematic literature reviews and research designs.

Because the Five-Factor Model arose from the convergence of several independent lines of research, there are several slightly different versions of the model, and a number of distinct operationalizations. Research in this Laboratory has used the Revised NEO Personality Inventory (NEO-PI-R), in which the five factors are each defined by six specific facet scales. This hierarchical feature of the NEO-PI-R means that personality can be described either in the broad terms of the 5 domains or at the detailed level of the 30 facets.

One focus of research has been a comparison of the NEO-PI-R system with alternative operationalizations of the Five-Factor Model and alternative taxonomies. One study examined two adjective-based measures of the Five-Factor Model. Although all five factors showed convergent validity, an examination of the particular NEO-PI-R facets with which the adjective measures best correlated showed subtle differences in the conceptualizations. A study comparing the NEO-PI-R to a multi-faceted version of Eysenck's Three-Factor Model demonstrated that the latter is not comprehensive, lacking the Openness factor. Another study examining Tellegen and Waller's Seven-Factor Model showed that the two additional factors of Positive and Negative Valence could be adequately interpreted within the NEO-PI-R system.

Stability and Change in Personality: Personality stability and change has been a longstanding interest in PSCS. We have reported longitudinal studies in men for intervals of up to 30 years using the Guilford-Zimmerman Temperament Survey or GZTS. Recently we reported analyses of GZTS scores in women over a 12-year interval that replicated the high levels of stability in individual differences seen in men. Mean levels of personality traits showed little change, although both men and women showed modest declines in General Activity after age 50.

We have also examined possible moderators of stability. In collaboration with Dr. Jeffrey Metter, BLSA Medical Officer, we examined stability in people whose clinically assessed physical health improved, declined, or stayed the same over 6-year periods. The results consistently showed no effects of physical health changes on levels of personality stability. These findings underscore the importance of personality changes when they do occur: They are apparently not normal aging, nor are they due to common physical diseases. They may be most important as early signs of Alzheimer's Disease, as noted in the Clinical Practice Guideline on Early Recognition and Initial Assessment of Alzheimer's Disease.

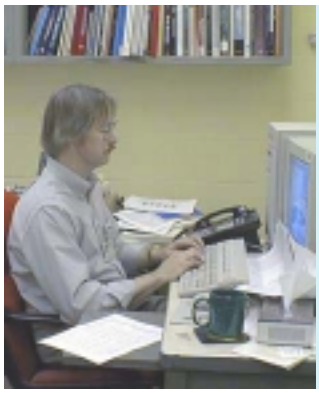
Stress, Coping, and Psychopathology: Personality traits are important determinants of the ways in which people deal with stress. For example,

Extraversion is associated with forms of coping that involve humor, talking about feelings, and seeking support; Agreeableness is associated with stoic and compliant attitudes in the face of stress. Our perspective integrates stress-and-coping research into the broader field of psychology, linked to normal adaptation, psychopathology, and the personality dimensions that affect all these.

Traditionally, normal and abnormal psychology were held to be distinct and qualitatively different. Our research has shown that in many respects they are closely related, and thus that knowledge from one field is relevant to the other. For example, some of our research has focused on depression. We have shown that depressive symptoms are related to the normal personality disposition Neuroticism, can be predicted years in advance from personality traits, and can themselves predict psychiatric diagnoses noted in hospitalization records. Perhaps most important, we have also shown that depressive symptoms and the personality traits that predispose people to depression do not increase as a normal consequence of aging. Most older people are not depressed, and those that are should receive appropriate treatment.

The Five-Factor Model and NEO-PI-R have stimulated a number of studies on the relation between normal personality traits and the personality disorders classified on Axis II of the DSM-IV. These studies led to an edited volume, published by the American Psychological Association, which includes articles on theory, research, and clinical applications of the Five-Factor Model in diagnosing and treating personality disorders. Currently we are extending the scope of this line of research by conducting a collaborative cross-cultural study of personality and personality disorders with colleagues from the Hunan Medical University in the People's Republic of China.

Collaborators: Michael H. Bond, Ph.D., Chinese University of Hong Kong; Sampo V. Paunonen, Ph.D., University of Western Ontario; Gergorio H. del Pilar, Jean-Paul Rolland, Ph.D., University of Paris X Nanterre; Wayne D. Parker, Ph.D., Stephanie V. Stone, Ph.D., Peter Fagan, Ph.D., Johns Hopkins University; Fritz Ostendorf, Ph.D., Alois Angleitner, Ph.D., University of Bielefeld; Margarida P. de Lima, Ph.D., Antoino Simoes, Ph.D., University of Coimbra; Iris Marusic, Ph.D., Denis Bratko, Ph.D., University of Zagreb; Gian Vittorio Caprara, Ph.D., Claudio Barbaranelli, Ph.D., University of Rome; Joon-Ho Chae, Ph.D., Sogang University; Ralph L. Piedmont, Ph.D., Loyola College of Maryland.; D. J. Vandenbergh, J. Wang, and George R. Uhl, NIDA; Gerald Matthews, University of Dundee; Donald H. Saklofske, University of Saskatchewan; Ian Deary, University of Edinburgh; Moshe Zeidner, University of Haifa.



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Recent Publications:

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McCrae RR, et al. *Psychol Bull* 1996; 120: 323-37.

McCrae RR, et al. *Dev Psychol* 1999; 35: 466-477.

Biography: Dr. McCrae received a B.A. in Philosophy from Michigan State University, and a Ph.D. in Personality Psychology from Boston University. After three years at the Normative Aging Study in Boston, he joined the NIA to become Research Psychologist and Senior Investigator for Personality, Stress, and Coping Section, Laboratory of Personality and Cognition. His work has been centered on studies of personality structure (the Five-Factor Model) and assessment (the Revised NEO Personality Inventory) and applications in health and aging.

Personality traits are dimensions of individual differences in the tendencies to show consistent patterns of thoughts, feelings, and actions. Traits are important because their influence is pervasive: They affect personal interactions and social support, health habits and somatic complaints, attitudes and values, ways of coping, occupational and recreational interests, and much more. For the past 14 years, research in this laboratory has utilized a particular version of trait structure, the Five-Factor Model, and an instrument developed to assess 30 specific traits that define the five factors, the Revised NEO Personality Inventory (NEO-PI-R). Work in the past year has emphasized basic research on the generalizability of the model, and special attention has been given to Openness to Experience, the least well understood of the five factors.

Cross-Cultural Studies of the Five-Factor Model: Cross-cultural studies are of immense importance in personality psychology, because the major variables thought to affect personality development—genetic inheritance, early family environment, and social structural variables such as class, political climate, and religious traditions—cannot feasibly or ethically be manipulated. Personality psychologists must depend on "natural experiments," and many of these are provided by comparing individuals across cultures.

Since the publication of the NEO-PI-R in 1992, researchers outside the U.S. have translated the instrument into over 20 different languages, and many have collected data for their own research purposes. In collaboration with these investigators, we have recently begun cross-cultural studies of personality structure and development. In the first of these we reported an analysis of personality structure in Hong Kong Chinese and Japanese samples. Using statistical methods developed in part in this Laboratory, we showed that the Five-Factor Model is well replicated in both these non-Indo-European languages. Subsequent research has extended this finding to several other languages—in fact, to date no study using an authorized translation, adequate sample size, and appropriate analysis has failed to replicate the five-factor structure of the NEO-PI-R. These data suggest that the Five-Factor Model may be a human universal.

American studies of adult personality development can be summarized by saying that three of the factors (Neuroticism, Extraversion, and Openness) decrease, whereas the other two (Agreeableness and Conscientiousness) increase with age; most of the change occurs between age 18 and age 30. These cross-sectional differences might reflect cohort effects attributable to the historical experience of different generations of Americans. But other nations have had very different histories during the same period, and if age differences are due to cohort effects, it is unlikely that the same kinds of age differences would emerge in cross-sectional studies in those countries. However, reanalysis of data provided by collaborators in five countries (Germany, Italy, Portugal, Croatia, and Korea) show very similar patterns of age differences, suggesting that these may perhaps best be interpreted as effects of intrinsic maturation.

One of the limitations of our research to date is that only relatively modern, industrialized nations have been sampled, and the NEO-PI-R has not been translated into any of the languages native to the Americas or Sub-Saharan Africa. To examine further the generalizability of the Five-Factor Model, we are planning a collaborative study of age and personality structure in Zimbabwe, using a translation of the NEO-PI-R into Shona, a Bantu language.

The Origins of Personality - Behavior Genetics: According to Five-Factor Theory, personality traits are endogenous basic tendencies. Genetic factors are expected to play a major role in their origin and development, whereas environmental factors like culture should play a minor role. In collaboration with Swedish researchers, we published one of the first studies on the heritability of Openness to Experience, and we are currently working with John Loehlin to reanalyze the classic National Merit Twin Study data for all five factors. A collaboration with behavior geneticists in Canada and

Germany suggests that the five factors are strongly heritable in both these two cultures. In addition, that study demonstrates that more narrow and specific facet-level traits are also substantially heritable. Thus, it appears that there is a genetic basis for many of the details of personality, as well as the broad outlines.

Studies of Openness to Experience: Openness to Experience is the least well understood of the five personality factors. Different versions of the factor have been labeled Culture, Inquiring Intellect, Imagination, and Independence of Judgment. As assessed by the NEO-PI-R, Openness is seen in Fantasy, Aesthetics, Feelings, Actions, Ideas, and Values, and is thus much broader than labels such as Intellect suggest.

Correlational studies in the BLSA have shown that Openness is empirically related to a wide variety of constructs, including Jung's Intuition, Hartmann's Thin Boundaries, Tellegen's Absorption, and Murray's Need for Sentience, as well as to corresponding factors in alternative measures of the Five-Factor Model (e.g., Goldberg's Intellect). It shows smaller, if still significant, correlations with measures of intelligence and divergent thinking ability.

This body of empirical findings has been used to develop a conceptualization of Openness with both motivational and structural aspects. Although Openness is essentially a matter of differences in the internal processing of experience, it has far-reaching consequences in social interactions. A review of the literature showed that Openness or related constructs were important for understanding cultural innovation, political ideology, social attitudes, marital choice, and interpersonal relations.

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Recent Publications:

Vandenbergh DJ, et al. *Mol Psychiatry* 1997; 2: 417-419.

Resnick SM, et al. *Neurology* 1997; 49: 1491-1419.

Maki PM, et al. *Psychol Aging* 1999; 14: 284-294.

Biography: Dr. Zonderman received his undergraduate degree in Behavior Genetics from University of Massachusetts and his doctorate in Psychology from the University of Colorado. After a postdoctoral fellowship in multivariate statistics at the University of California, Berkeley, and academic positions at University of California, Davis and The Johns Hopkins University, he joined NIA as a Senior Staff Fellow in the Stress and Coping Section. Since 1997, he has been Chief of the Cognition Section in the Laboratory of Personality and Cognition. His research interests include individual differences in cognition and personality and their relationship with adult morbidity and mortality, predicting the onset of cognitive impairments and Alzheimer's disease, and the role of genetics in cognitive declines and personality.

Distinguishing Pathological from Normal Cognitive Aging: Research in the Cognition Section focuses on distinguishing pathological from normal cognitive aging. The purpose of this research is to identify predictors of cognitive morbidity, and to identify which cognitive processes are preserved with aging and which processes are vulnerable to disease. The primary effort of research in the Cognition Section is focused on longitudinal research in the Baltimore Longitudinal Study of Aging (BLSA). Cognitive tests have been administered to participants in the BLSA since 1960. Some individuals presently in the study have as many as seven repeated assessments beginning in the 1960's.

The cognitive tests administered to participants in the BLSA reflect our primary interest in pathological cognitive impairments, especially Alzheimer's disease (AD). The cognitive testing program is divided into two batteries, one for longitudinal prediction and another for cognitive and neuropsychological outcomes. The longitudinal repetitions of these tests distinguish typical changes in performance associated with aging from changes in performance which may be associated with disease when combined with neurological and neuropsychological outcomes and clinical diagnoses of AD.

An increasingly important area of research in the Cognition Section focuses on factors that reduce the risk of cognitive declines. An example of this focus is the finding that nonsteroidal anti-inflammatory drugs reduce the risk of Alzheimer's disease. Another example of this focus is based on recent findings that estrogen replacement therapy reduces the risk for both AD and cognitive declines in post-menopausal women. In an intervention study testing the effects of hormone replacement on cognition, we are examining the effects of estrogen and testosterone in older women and men in conjunction with structural and functional neuroimages.

Cognitive Declines in Aging Subjects Free of Dementing Diseases: In people with no signs of dementia, some cognitive abilities resist decline while other abilities show characteristic age-related changes beginning in the 50's or 60's. Research by investigators in the Cognition Section has shown that vocabulary scores generally resist declines, and may increase slowly over time until there are small decreases after the eighth or ninth decades. Immediate visual memory shows a much different pattern of change. We found that errors in immediate visual recall increased exponentially with increased age in both cross-sectional and longitudinal analyses

We also found that there were different rates of change in separate types of errors over time. Distortions, rotations, perseverations and mislocations were the most frequent errors across all ages. Although older participants made significantly greater errors regardless of error type, the greatest age differences were found for distortions and omissions. Men and women showed similar patterns of age-associated increases in errors, but there was a significant interaction between gender and error type indicating that women across all ages made more omissions and rotations, not other types of errors. Longitudinal analyses showed that distortions, omissions and rotations increased with age. Although women made more omission errors, men showed steeper increases with age.

Long-Term Predictions of Cognitive Impairment and Dementia: The onset of cognitive impairment is either a discrete event or a gradual process that manifests over time. We asked whether changes in previous test performance predict evidence of cognitive impairment assessed by the Mini-Mental Status Examination (MMSE) over relatively long intervals. We hypothesized that visual memory administered prior to the MMSE would significantly account for cognitive impairment after controlling for age at mental status exam and vocabulary score (a measure highly related to general intelligence). The correlations between visual memory and MMSE over 6-8 and 9-15 years were .36 and .34 ($p < .05$). These results provide preliminary evidence that mental status can be predicted, at least in part, by earlier performance on cognitive tests. Although the present findings are limited to only these cognitive tests, they provide important evidence that early signs of dementia may be detectable as many as 6-15 years prior to noticeable decline on mental status tests.

Six-year changes in immediate visual memory predicted Alzheimer's disease (AD) prior to its onset. Individuals with diagnoses of AD had larger changes in immediate memory performance over the six-year interval prior to the estimated onset of their disease than subjects without AD. Six-year longitudinal change in immediate visual memory performance also predicted subsequent cognitive performance 6-15 and 16-22 years later, even after adjusting for the influences of age, general ability, and initial immediate memory. These results provide evidence that change in immediate visual memory performance has long-term prognostic significance. These results further suggest that change in recent memory performance may be an important precursor of the development of the disease.

Analyses comparing BLSA participants who developed dementing illnesses with nondemented participants also showed that particular errors in visual memory may be more sensitive markers of impairment than others. More than 5 years before the onset of illness, demented individuals made more distortion errors than participants who did not develop dementing illnesses. In addition, individuals with signs of dementia had significantly greater rates of change in perseverations, rotations, and size errors compared with nondemented participants. These findings suggest that immediate visual memory is an important test for distinguishing normal from pathological cognitive decline and that specific types of errors in short-term memory may be important early markers of dementia.

Risks and Protective Factors for Cognitive Decline: If cognitive decline is an important predictor of pathological cognitive aging then it seems reasonable to investigate factors that decrease or increase the risk of cognitive decline. Estrogen replacement therapy (ERT) is increasingly

recommended for postmenopausal women due to its potential beneficial effects on physical health in older women. The possibility of a protective effect on cognitive function has also been suggested. In the BLSA, women receiving hormone treatment at the time of testing made significantly fewer errors in immediate visual recall than women who were not on hormone therapy. Less memory change was found in women who started hormone therapy between examinations than women who never received hormone therapy. These findings support the notion that estrogen has a beneficial role on cognitive functioning in aging women.

We continue to extend our present studies on the risks and protective factors for cognitive declines and dementias. In particular, as we gather additional repeat data on which to base reliable measures of cognitive trajectories, we will relate apoE and other genotypic and genomic measures to determine whether there are critical periods of decline. In addition, we will examine the role of modulators of cognitive decline such as hypertension and hormone replacement therapy, particularly in conjunction with MRI anatomical and PET functional assessments. We will also examine chronicity of hypertension, adequacy of blood pressure control, and differential effects and interactions with other known risks such as apoE genotype.

Collaborators: Claudia H. Kawas, M.D., Johns Hopkins Bayview Medical Center; R. Nick Bryan, M.D. Ph.D., Johns Hopkins University; David. J. Vandenbergh, Pennsylvania State University.

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Recent Publications:

Resnick S, et al. *Horm Behav* 1998; 34: 171-182.

Davatzikos C, et al. *Cereb Cortex* 1998; 8: 635-640.

Biography: Dr. Resnick received her Ph.D. in Differential Psychology and Behavioral Genetics from the University of Minnesota and completed a postdoctoral fellowship in Neuropsychology and Neuroimaging at the University of Pennsylvania. She was Research Assistant Professor of Psychology in Psychiatry at the University of Pennsylvania prior to joining the Laboratory of Personality and Cognition, NIA in 1992. She studies brain-behavior associations in health and disease and is currently the principal investigator of the brain imaging component of the Baltimore Longitudinal Study of Aging. This longitudinal neuroimaging study focuses on early structural and physiological brain changes that may be associated with memory and cognitive change in older individuals.

Brain Changes as Predictors of Cognitive and Memory Decline: The goal of our research program is to identify brain changes which may predict cognitive and memory decline in older individuals. We use magnetic resonance imaging (MRI) to measure the structure of the brain and positron emission tomography (PET) to measure changes in regional cerebral blood flow (rCBF) during the performance of memory tasks and over time.

Early Markers of Alzheimer's Disease - Brain Changes in the Baltimore Longitudinal Study of Aging (BLSA): We are performing a 9-year neuroimaging study involving annual MRI and PET scans and neuropsychological evaluations in selected BLSA participants aged 55 and older. This longitudinal design provides a sensitive to way to investigate the relationship between changes in brain structure and physiology and decline in memory and cognition. Furthermore, using the wealth of prior psychological and medical information available for BLSA participants, including as many as 8 prior memory assessments over more than 30 years, we are able to examine trajectories of cognitive aging in relation to individual differences in the brain years later. To date, approximately 160 individuals (90 men, 60 women) have enrolled in the brain imaging study, and recruitment of additional women is still ongoing.
The specific goals of this study are: to determine the rate of brain changes

with age, including increases in brain atrophy and vascular abnormalities; to determine the association between trajectories of memory and cognitive change and changes in brain structure and function; and to determine whether risk and protective factors, such as hormone replacement therapy, use of non-steroidal anti-inflammatory agents, and vitamins, modulate these relationships. An understanding of the associations between brain and neuropsychological changes, as well as early detection of these changes, will be critical in identifying individuals likely to benefit from new interventions in preventing and treating Alzheimer's Disease and other memory problems in the elderly.

Preliminary results are available for the first 2 years of our longitudinal brain imaging study. MRI data are analyzed using qualitative ratings and quantitative analysis of volumetric images. Results of the qualitative ratings, which are accomplished using the procedures developed and validated as part of the Cardiovascular Health Study, indicate significant effects of age and sex on atrophy ratings, with greater brain atrophy in older compared with younger participants and in men compared with women. Ratings of white matter hyperintensities (WMH), which reflect ischemic and/or demyelinating findings show more extensive WMH in older subjects, but no differences between men and women in this age range (55-85).

A great deal of effort in our laboratory has focused on the development of an image processing approach which provides accurate and valid segmentation and quantification of gray and white matter, and cerebral spinal fluid volumes. Quantitative analysis of regional brain volumes for subjects who have completed 2 evaluations reveals significant effects of age and sex on brain volumes and ventricular volumes. The cross-sectional findings from the Year 1 MRI scans indicate less gray and white matter volume and more ventricular CSF in older compared with younger participants; the magnitude of these findings is different across frontal, parietal, temporal and occipital brain regions. Consistent with previous studies and our atrophy ratings, men have greater ventricular CSF volumes. There are no detectable changes in lobar brain volumes over a one-year period, but there was a small but significant increase in the volume of the ventricles.To determine whether early blood flow changes can be used as predictors of cognitive and memory change, we are performing PET-rCBF studies as part of our BLSA neuroimaging study. PET rCBF scans are obtained under three conditions: during rest and the performance of verbal and figural continuous recognition tasks. This procedure is conceptualized as a cognitive stress test to examine age-associated changes in rCBF during increased demand. We have described pixel-based maps of the associations between age and resting rCBF (normalized for global CBF). The correlation maps demonstrate significant negative correlations between age and CBF in

the insular and superior temporal regions, and in visual association cortex (Areas 18 and 19) bilaterally for both men and women. Significant positive correlations between age and relative rCBF were observed for both men and women in subcortical, sensorimotor regions, and superior frontal gyrus. To our knowledge, this sample represents the largest study of associations between age and regional CBF studied with PET and provides a detailed map of age differences in blood flow during a period of accelerating cognitive and memory decline.

Effects of Estrogen on Cognitive Decline: We are also investigating the potential modulatory role of hormone replacement therapy on Alzheimer's Disease and cognitive and memory decline in older women. We have shown that women in the BLSA who had ever used estrogen replacement therapy had a reduced risk of developing Alzheimer's Disease in comparison with women who had never used hormone therapy. We have also shown that nondemented women in the BLSA who were using estrogen replacement therapy performed better on a test of short-term memory for designs compared with never-users. In a small subgroup of women with memory assessments prior to and following initiation of hormone treatment, the estrogen therapy appeared to protect against age-associated decline in memory.

Future Directions: Our future work will emphasize continuation of the longitudinal neuroimaging study, including continued acquisition of annual evaluations, further analyses of existing imaging and neuropsychological data, development of new approaches for longitudinal analyses of functional images, and examination of modulating factors on the relationship between brain and neuropsychological changes. In addition, we have begun intervention studies to examine the effects of suggested protective agents, such as sex steroid hormones, on brain structure and function.The data collected over the first 2 years of the study indicate only small changes over one year in regional brain volumes and ventricular CSF. In contrast, the cross-sectional age differences between younger and older participants are 5 to 7% in frontal and temporal volumes and 51% in ventricular volume. It will be critical to continue repeated evaluations of our participants to examine the rate and regional pattern of longitudinal age changes.

Another important area of future research, which has only recently received attention in the brain imaging literature, is the role of modulatory factors on measurement of brain structure and function. We plan to examine suggested risk and protective factors in relation to brain changes, neuropsychological changes and their association. For example, data on family history for Alzheimer's Disease and related disorders, apolipoprotein E genotype, head trauma, history of hypertension, use of estrogen replacement therapy, and use of non-steroidal anti-inflammatory agents will be examined as potential

modulators of the relationship between brain and neuropsychological changes.

Ongoing and future work will include intervention studies to examine suggested protective agents, such as estrogen and testosterone, on brain structure and function. Dr. Pauline Maki, an NRC fellow in our laboratory, is conducting a double-blind placebo-controlled study of estrogen and testosterone effects on cognition and mood in older women and men, respectively. In addition, we will perform MRI and PET studies to investigate concomitant effects on brain structure and regional cerebral glucose metabolism.

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Recent Publications:

Thayer JF, et al. *Biol Psychiatry* 1998; 44: 304-306.

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Biography: Dr. Thayer received a B.A. in Psychology from Indiana University, and Master's and Ph.D. degrees from New York University. After academic positions at Penn State University and the University of Missouri, he joined NIA to initiate a program on Emotions and Quantitative Psychophysiology. His research interests concern biological and psychological adaptation and flexibility in the context of dynamical systems models with applications to psychopathology, pathophysiology, and health. This work utilizes indices of autonomic nervous system function derived from cardiac variability measures to probe whole organism systems.

Heart Period Variability as an Index of Neurovisceral Integration: One aspect of our research program is to develop, elaborate, and apply a model of neurovisceral integration in the context of normal and pathological functioning. This model uses heart period variability (HPV) to index the functioning of central-peripheral feedback mechanisms that produce goal-directed behavior. We have related HPV to attentional regulation and affective regulation in humans. These studies suggest that autonomic, attentional, and affective regulation are coordinated in the service of system adaptability and goal-directed behavior.

Autonomic Characteristics of Anxiety and Mood Disorders: Anxiety and depression are disorders associated with somatic symptoms such as tachycardia, rapid breathing, and disturbed sleep. Moreover, anxiety and depression are risk factors for cardiovascular morbidity and mortality. Our research has focused on the autonomic characteristics on these disorders to investigate their physiological and psychological concomitants with an eye toward understanding their development, course, and treatment. Research to date indicates that these disorders are associated with a relative decrease in vagally mediated cardiovascular control. This lack of cardiac vagal control is associated with poor affective and attentional regulation. Importantly, these deficits normalize with therapeutic intervention.

Cardiovascular Variabilities and Health: We are examining the relationship between HPV and cardiovascular system control. This research suggests that HPV and blood pressure variability (BPV) are inversely related in the healthy, intact organism and serves to maintain adequate blood pressure control. In spinal cord injury, the relationship between HPV and BPV can become dysfunctional, leading to poor blood pressure regulation and increased risk for cardiovascular disorders.

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